Response to Neoadjuvant Chemoradiotherapy in a Patient with Mucinous Adenocarcinoma Arising from a Chronic Anorectal Fistula and Diagnosed by Transrectal Punch Biopsy: A Case Report

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Mucinous adenocarcinoma arising from a chronic anorectal fistula is a rare condition. It is often confused with a hemorrhoid or perineal abscess, which consequently delays accurate diagnosis. Here, we report the case of a 58-year-old man with blood-tinged stool who reported a rectal mass, which was diagnosed as mucinous adenocarcinoma arising from an anal fistula. After initial computed tomography-guided needle aspiration biopsy had failed to provide an accurate diagnosis, transrectal punch biopsy was performed to obtain adequate tissue sample for confirmative histological diagnosis. The patient was successfully treated with neoadjuvant concurrent chemoradiotherapy followed by surgical intervention. (Intest Res 2013;11:306-309)

Key Words: Adenocarcinoma, mucinous; Rectal fistula; Neoadjuvant therapy; Chemoradiotherapy

INTRODUCTION

Mucinous carcinomas refer to those composed of more than 50% extracellular mucin. Generally, mucinous carcinomas of the colon and rectum develop in young patients. They are more frequently found in the proximal colon and are usually in advanced stages at the time of diagnosis. In addition, they are associated with a high incidence of local and distant metastasis, with worse prognosis than usual adenocarcinoma.1 Malignant transformation of chronic anal fistula to mucinous adenocarcinoma is a rare condition, accounting for up to 0.1% of all colorectal adenocarcinomas.2 Mucinous adenocarcinoma in the anal region is often confused with a hemorrhoid or perineal abscess, and therefore, early diagnosis is difficult.3 Moreover, there is a lack of standard manage-
total bilirubin, 0.5 mg/dL; total protein, 6.9 g/dL; albumin, 3.9 g/dL; calcium, 8.6 mg/dL; inorganic phosphate, 3.2 mg/dL; uric acid, 4.2 mg/dL; ALP, 91 IU/L; sodium, 140 mmol/L; potassium, 4.2 mmol/L; chloride, 102 mmol/L; total carbon dioxide, 28 mmol/L; PT (INR) 12.6 seconds (99%), and aPTT, 34.7 seconds. CT showed wall thickening of the rectum and a perirectal lesion with increased attenuation on the right posterior aspect. Colonoscopy suggested rectal edema around a fistula opening (Fig. 1A). MRI evidenced a 4.2×3.5-cm mass on the right side of the rectal wall. The mass consisted of a mucin pool and arose from the perianal fistula, with enhancement on the right side of the lower mesorectum, right levator ani, and soft tissue infiltration to the prostate and seminal vesicles (Fig. 1B, C). Colonoscopic biopsy showed hyperplastic polyps, and CT-guided needle aspiration biopsy only showed fibrous tissues with dissecting mucin but not epithelial components, suggesting a malignant pathology for the rectal lesion. To accurately confirm tissue diagnosis, transrectal punch biopsy was performed at the position that was hard on palpation during rectal examination. The histological diagnosis after transrectal punch biopsy was moderately differentiated adenocarcinoma (T4N0M0, stage III) (Fig. 1E).

Neoadjuvant therapy consisting of chemotherapy with 5-fluouracil and leucovorin for 4 months, and preoperative radiotherapy with 50.4 Gy in 25 fractions for 1 month was administered. MRI assessment of response to neoadjuvant therapy was performed upon treatment completion. The primary mass size was decreased from 4.2×3.5 cm to 4.0×2.9 cm and previously noted strong fluorodeoxyglucose uptake on PET-CT scans in the upper rectum was no longer present (Fig. 2A, B). The serum CEA level also decreased from 20.8 to 3.6 ng/mL. Four weeks after concurrent chemoradiotherapy completion, the patient underwent abdominoperineal resection (Miles operation) with lymph node dissection and radical prostatectomy. The abdominoperineal resection specimen was 25 cm in length. A firm lesion measuring 5.0×5.0 cm within the fistula tract was present at 3 cm above the anal verge (Fig. 2C). Final pathological study of the surgical specimen revealed mucinous adenocarcinoma with prominent mucin pool formation and rare residual cancer cells because of preoperative chemoradiotherapy (Mandard grade 2) (Fig. 2D, E). Tumor invasion up to the perirectal fat tissue was noted, with negative resection margins. No lymphovascular invasion or perineural invasion (T3N0M0, Stage II) was
noted. The patient was discharged from the hospital 8 days after surgery without any complications. He then completed postoperative adjuvant chemotherapy.

**DISCUSSION**

Mucinous adenocarcinoma associated with chronic fistula in the anus is very rare and difficult to be diagnosed.\(^4\)\(^,\)\(^5\) It means this cancer is difficult to be diagnosed accurately. And it is easy to be confused with hemorrhoid and perineal abscess. In addition, accurate diagnosis is usually delayed because (1) symptoms like anal pain, anal discharge, and anal fistula can also be caused by benign anal diseases and (2) mucinous adenocarcinomas are not regularly detected using common forceps biopsy procedures because of their infrequent involvement of the rectal mucosa.\(^6\)

MRI has been considered the most accurate preoperative technique for detecting the mucin pool of mucinous adenocarcinomas.\(^7\) Pathological confirmation is however necessary for treatment. Therefore, when CT\(^8\) or colonoscopy-guided needle aspiration biopsy fails to provide a histological diagnosis, other options need be explored.

Punch biopsy, despite being more invasive than fine needle aspiration biopsy, is a commonly performed diagnostic procedure on abnormal skin lesions and the gold standard for early detection of prostate cancer. Diagnostic accuracy can be significantly improved using punch biopsy without an obvious increase in the complication rate.\(^8\) Cells obtained from a fine needle aspiration biopsy are collected randomly into the needle and thus observed microscopically as a disorganized cell clutter. However, punch biopsy with the larger needle allows the cells to be removed as an intact structure.

It is often difficult to determine the pathology of these tumors because they usually also consist of normal structure, mucin fluid, and inflammatory tissue at the time of presentation.\(^3\) Consequently, most mucinous adenocarcinoma cases are confirmed by excision biopsy and thus diagnosis is delayed. In this case, transrectal punch biopsy proved to be diagnostically effective and accurate, and therefore should be considered as an option for mucinous adenocarcinoma diagnosis.

Surgical resection is the first choice for curative treatment of anal adenocarcinoma, including mucinous carcinoma. In most cases of anal mucinous adenocarcinoma, surgery precedes chemotherapy or radiotherapy, and the role of radiotherapy alone or in combination with chemotherapy...
has not been established for perianal mucinous carcinoma. Moreover, a few case reports advocate the use of chemoradiation therapy prior to surgery, but the literature in this regard is scarce. It means there is no difference in survival rates between mucinous adenocarcinoma and adenocarcinoma when treated by preoperative chemotherapay and radiotherapy. In accordance with these guidelines, we treated the patients with combined radiotherapy and chemotherapy and demonstrated that neoadjuvant chemoradiotherapy was effective in reducing tumor size and surgical stage in this case of mucinous adenocarcinoma.

In conclusion, our experience with this case suggests that punch biopsy is a novel diagnostic option and that neoadjuvant chemoradiotherapy followed by surgery may play an important role in the treatment of perianal mucinous carcinoma.

REFERENCES